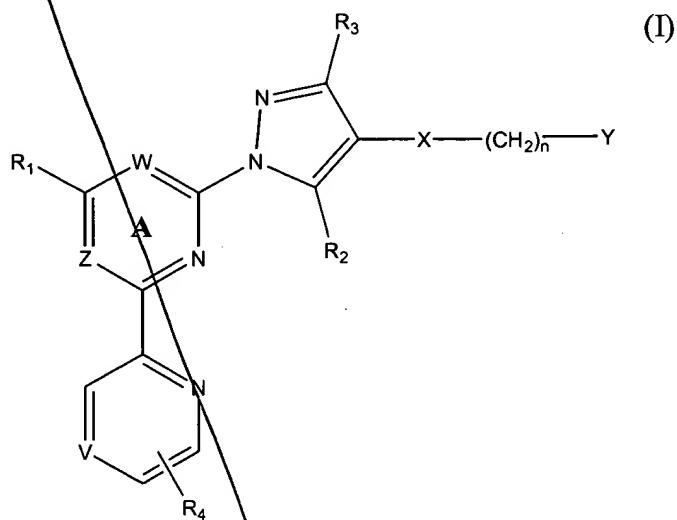


CLAIMS

What is claimed is:

1. A compound of Formula I,



5

and physiological salts thereof, wherein:

n is 0, 1 or 2;

X is O, CH₂, S or SO₂;

R₁ is H or NH₂;

10 R₂ and R₃ are each, independently, -H, -OH, a substituted or unsubstituted alkyl, or a substituted or unsubstituted alkoxy;

R₄ is, -H or a substituted or unsubstituted alkyl;

V, W and Z are each, independently, N or CH; and

Y is selected from the group consisting of substituted and unsubstituted phenyl, substituted and unsubstituted heterocycl.

2. The compound of Claim 1, wherein Y is a phenyl group which has one or more substituents independently selected from the group consisting of halogen, linear or branched C₁-C₄-alkoxy, trifluoromethoxy, dioxymethylene, hydroxyalkyl, trifluoromethyl, HC(O)-, linear or branched C₁-C₄-alkyl, heterocycl and substituted or unsubstituted heterocycloalkylalkyl.

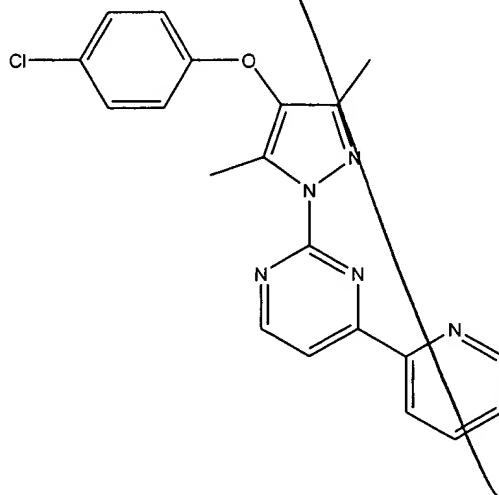
5

3. The compound of Claim 2, wherein Y is a phenyl group which has one or more substituents selected from the group consisting of fluoro, chloro, methoxy, morpholyl, N-morpholinomethyl, tetrahydroisoquinolyl, tetrahydroisoquinolinomethyl, 4-(4-benzyl-piperazin-1-yl)methyl, 4-(4-(2-fluoro-phenyl)piperazin-1-yl)methyl, and isopropyl.

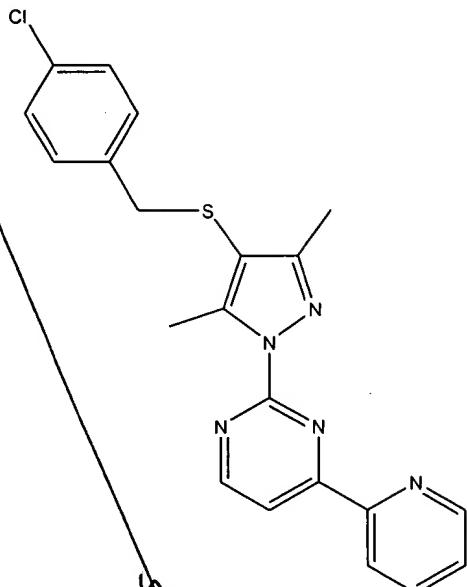
10

4. The compound of Claim 1, wherein Y is selected from the group consisting of pyridyl, furyl, and pyrrolidyl.

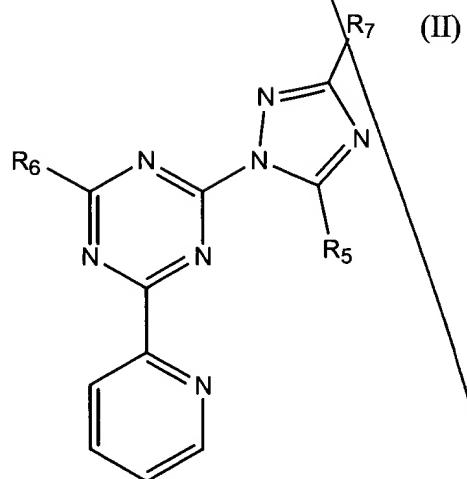
15 5. A compound represented by the following structural formula:



6. A compound represented by the following structural formula:



7. A compound of Formula II,



and physiological salts thereof, wherein,
R₅ is substituted or unsubstituted aralkyl, substituted or unsubstituted cycloalkyl, or substituted or unsubstituted cycloalkylalkyl;
R₆ is -H or -NR₁₃R₁₄;
5 R₇ is substituted or unsubstituted phenyl; and
R₁₃ and R₁₄ are each, independently, -H, a substituted or unsubstituted alkyl, a substituted or unsubstituted cycloalkyl, a substituted or unsubstituted aryl, a substituted or unsubstituted aralkyl; or
10 R₁₃ and R₁₄ together with the nitrogen to which they are attached are a heterocycloalkyl.

8. The compound of Claim 7, wherein R₅ is substituted or unsubstituted benzyl.

9. The compound of Claim 8, wherein R₅ is benzyl having one or more substituents independently selected from the group consisting of halogen, linear C₁-C₄-alkoxy and branched C₁-C₄-alkoxy.

15 10. The compound of Claim 9, wherein R₅ is benzyl having one or more substituents independently selected from the group consisting of chloro and methoxy.

11. The compound of Claim 7, wherein R₅ is C₃-C₈-cycloalkyl, C₃-C₈-cycloalkyl-C₁-C₄-alkyl or substituted or unsubstituted phenyl-C₂-C₄-alkyl.

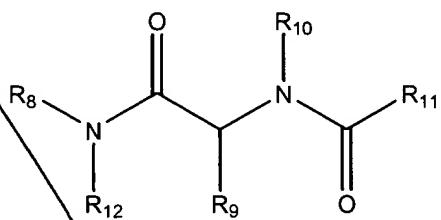
12. The compound of Claim 11, wherein R₅ is selected from the group consisting of 2-phenethyl, cyclohexyl and cyclopentylethyl.

20 13. The compound of Claim 7, wherein R₇ is phenyl having one or more substituents independently selected from the group consisting of halogen, linear C₁-C₆-alkyl, branched C₁-C₆-alkyl, cyclic C₃-C₆-alkyl and trifluoromethyl.

14. The compound of Claim 13, wherein R₇ is phenyl having one or more substituents independently selected from the group consisting of fluoro, chloro, linear C₁-C₄-alkyl, and branched C₁-C₄-alkyl.

15. A compound of Formula III,

5



(III)

*Sy
A*

and physiological salts thereof, wherein:

R₈ and R₁₂ are each, independently, -H, a substituted or unsubstituted alkyl, a substituted or unsubstituted aryl, substituted or unsubstituted aralkyl or a substituted or unsubstituted heteroaralkyl;

10 R₉ is -H, a substituted or unsubstituted aryl, a substituted or unsubstituted aralkyl, a substituted or unsubstituted heteroaryl or a substituted or unsubstituted heteroaralkyl;

R₁₀ is substituted or unsubstituted alkyl, a substituted or unsubstituted aryl, a substituted or unsubstituted heteroaralkyl, or a substituted or unsubstituted heterocycloalkylalkyl; and

15 R₁₁ is a substituted or unsubstituted alkyl, a substituted or unsubstituted aryl, a substituted or unsubstituted aralkyl, a substituted or unsubstituted cycloalkylalkyl, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted heteroaralkyl, a substituted or unsubstituted benzophenone, or a substituted or unsubstituted cycloalkylalkyl.

Sub
A1

16. The compound of Claim 15, wherein one of R₈ or R₁₂ is -H and the other is substituted or unsubstituted phenyl, phenyl-C₁-C₄-alkyl, diphenyl-C₁-C₄-alkyl, linear C₁-C₁₂-alkyl, branched C₁-C₁₂-alkyl, cyclic C₃-C₁₂-alkyl, or dicycloalkyl-C₁-C₄-alkyl.

5 17. The compound of Claim 16, wherein one of R₈ or R₁₂ is -H and the other is phenyl, phenyl-C₁-C₄-alkyl, or diphenyl-C₁-C₄-alkyl wherein the phenyl group or phenyl groups bear one or more substituents independently selected from the group consisting of C₁-C₄-alkoxy, C₁-C₄-alkyl and cyano.

18. The compound of Claim 17, wherein the phenyl group or phenyl groups bear one or more substituents independently selected from the group consisting of methoxy, methyl, ethyl and cyano.

10 19. The compound of Claim 15, wherein R₈ is selected from the group consisting of 2,2-diphenylethyl, 2-(4-ethylphenyl)ethyl, benzyl, diphenylmethyl, 1,2-diphenylethyl, 3,3-diphenylpropyl, 3,4,5-trimethoxybenzyl, 2,4,4-trimethylisopentyl, 2-(4-methoxyphenyl)ethyl, 2-cyclopentyl-2-phenylethyl, or 2-phenyl-2-pyridylethyl.

15 20. The compound of Claim 15, wherein R₉ is substituted or unsubstituted phenyl, substituted or unsubstituted phenyl-C₁-C₄-alkyl, diphenyl-C₁-C₄-alkyl, phenylfuranyl or heteroaryl-C₁-C₄-alkyl.

20 21. The compound of Claim 20, wherein R₉ is phenyl, phenyl-C₁-C₄-alkyl, diphenyl-C₁-C₄-alkyl wherein the phenyl group or phenyl groups bear one or more substituents independently selected from the group consisting of cyano, C₁-C₄-alkyl-S-, a halogen, a halogenated C₁-C₄-alkyl, C₁-C₄-alkoxy, trifluoromethyl, and substituted and unsubstituted phenoxy.

22. The compound of Claim 20, wherein R₉ is phenyl, phenyl-C₁-C₄-alkyl, diphenyl-C₁-C₄-alkyl wherein the phenyl group or phenyl groups bear one or more substituents independently selected from the group consisting of cyano, methyl, methoxy, phenoxy, chloro-substituted phenoxy, methoxy-substituted phenoxy and methyl-substituted phenoxy.

5

23. The compound of Claim 15, wherein R₉ is phenyl, 2-cyanophenyl, 3-cyanophenyl, 4-cyanophenyl, diphenylmethyl, pyrazolylmethyl, 2,4-dimethylphenyl, 2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 2-methyl-4-methoxyphenyl, 3-methyl-4-methoxyphenyl, 4-methylthiophenyl, 3-chlorophenyl, 3-trifluoromethylphenyl, benzyl, 2-trifluoromethylbenzyl, 3-trifluoromethylbenzyl, 2-chlorobenzyl, 3-chlorobenzyl, 4-chlorobenzyl, 2-methoxybenzyl, 3-methoxybenzyl, 4-methoxybenzyl, 2-fluorobenzyl, 3-fluorobenzyl, 4-fluorobenzyl, 3-azidylphenyl, 3-(4-methoxyphenoxy)phenyl, or 15 5-phenylfuran-2-yl.

10

24. The compound of Claim 15, wherein R₁₀ is substituted or unsubstituted phenyl, alkyl substituted with a heteroaryl group, alkyl substituted with a heterocycloalkyl group, or an alkyl substituted with -NR₁₃R₁₄, wherein:

Sub
A2

20 R₁₃ and R₁₄ are each, independently, -H, a substituted or unsubstituted alkyl, a substituted or unsubstituted cycloalkyl, a substituted or unsubstituted aryl, a substituted or unsubstituted aralkyl; or

R₁₃ and R₁₄ together with the nitrogen to which they are attached are a heterocycloalkyl.

25. The compound of Claim 24, wherein R₁₀ is 2-(imidazol-4-yl)ethyl, 3-(imidazol-4-yl)propyl, 3-(imidazol-1-yl)propyl 2-(3-methylimidazol-4-yl)ethyl, 2-(morpholin-4-yl)ethyl, 2-(4-pyrazolyl)ethyl, 4-pyrazolylmethyl, 2-N,N-dimethylaminoethyl, 3-N,N-dimethylaminopropyl, or 2-(aminocarbonyl)phenyl.

26. The compound of Claim 15, wherein R₁₁ is a linear or branched C₁-C₄-alkyl, substituted or unsubstituted phenyl, substituted or unsubstituted benzophenonyl, pyrazolyl, aminopyrazolyl, substituted or unsubstituted indolyl-C₁-C₄-alkyl, thiophenyl, quinoxaline, substituted or unsubstituted phenyl-C₁-C₄-alkyl, 5 pyridylcarbonylphenyl, phenylcarbonyl-C₁-C₄-alkyl, naphthyl, naphthyl-C₁-C₄-alkyl, diphenyl-C₁-C₄-alkyl, C₅-C₈-cycloalkyl-C₁-C₄-alkyl, C₁-C₄-alkylcarbonyl-C₁-C₄-alkyl, fluorenlyl, pryrrolyl, N-methylpyrrolyl, or pyridyl.

27. The compound of Claim 26, wherein R₁₁ is a phenyl, phenyl-C₁-C₄-alkyl, phenylcarbonyl-C₁-C₄-alkyl, naphthyl-C₁-C₄-alkyl, diphenyl-C₁-C₄-alkyl, C₅-C₈-10 cycloalkyl-C₁-C₄-alkyl, fluorenlyl or pyridyl substituted with one or more substituents independently selected from C₁-C₄-alkyl and C₁-C₄-alkoxy.

28. The compound of Claim 26, wherein R₁₁ is a benzophenonyl group, wherein said benzophenonyl group is substituted with a C₁-C₄-alkoxy group, a C₁-C₄-alkyl group or a chlorine atom.

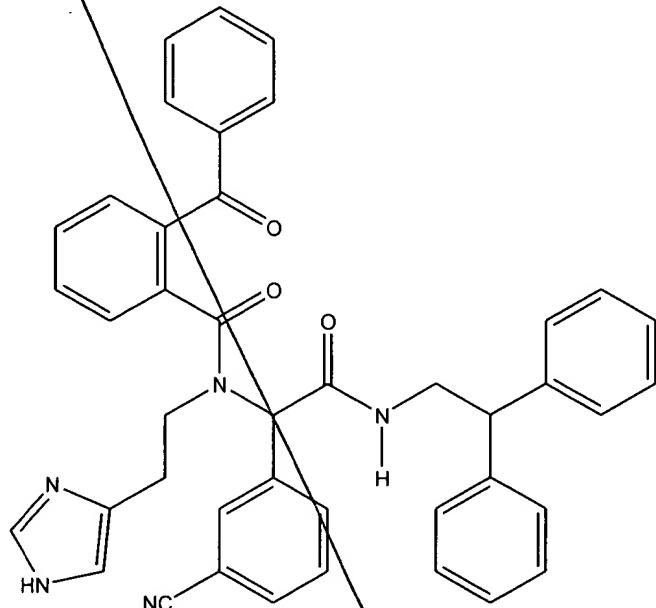
15 29. The compound of Claim 15, wherein R₁₁ is benzophenon-2-yl, 4'-methoxybenzophenon-2-yl, 4'-chlorobenzophenon-2-yl, 2-(furan-2-yl)phenyl, 2-(thiophen-2-yl)phenyl, 2-benzylphenyl, 2-pyridylcarbonylphenyl, 2-(phenoxyethyl)phenyl, 2-(t-butylcarbonyl)phenyl, 2,2-diphenylethyl, 1-fluorenlyl, (naphth-2-yl)methyl, naphth-1-yl, 3-(phenylcarbonyl)propyl, 4-phenylbutyl, 4-butylphenyl, 2-(4-chlorophenylcarbonyl)phenyl, 3-methoxyphenyl, N-methylpyrrol-2-yl, 2,3-dimethoxyphenyl, 3-butyl-2-pyridyl, 2-naphthylmethyl, 2-cyclohexylethyl, 3-methoxyphenyl, N-methyl-2-pyrrolyl, 2-cyclopentylethyl, 3-oxobutyl, 2-benzopyrazyl, quinoxalin-2-yl, 3-idolyl, (2-methylindol-3-yl)methyl, 3-(indol-3-yl)propyl, (indol-3-yl)methyl, (5-bromoindol-3-yl)methyl, 3-chlorophenyl, 3-aminopyrazol-4-yl, 2-(indol-3-yl)-1-20 25

hydroxyethyl, 3-fluorophenyl, 1-phenyl-1-hydroxymethyl, 2-phenylphenyl, 2-phenoxyphenyl, thiophen-2-yl, or isopropyl.

30. A composition of matter comprising an enantiomeric mixture of a compound represented by the following structural formula:

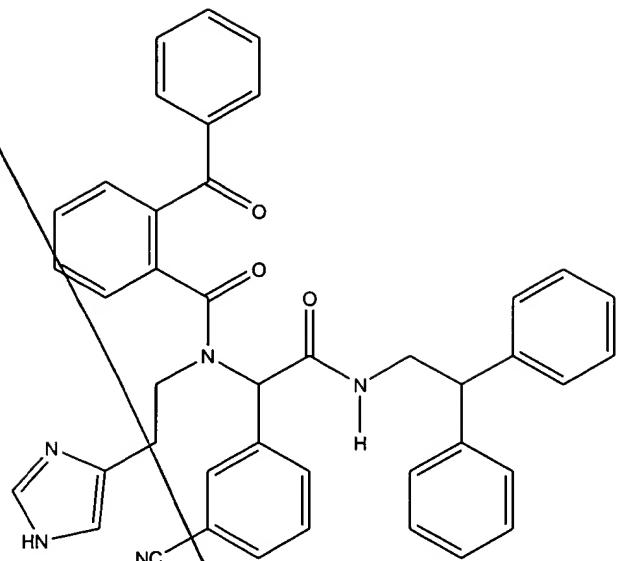
5

Sub
A3



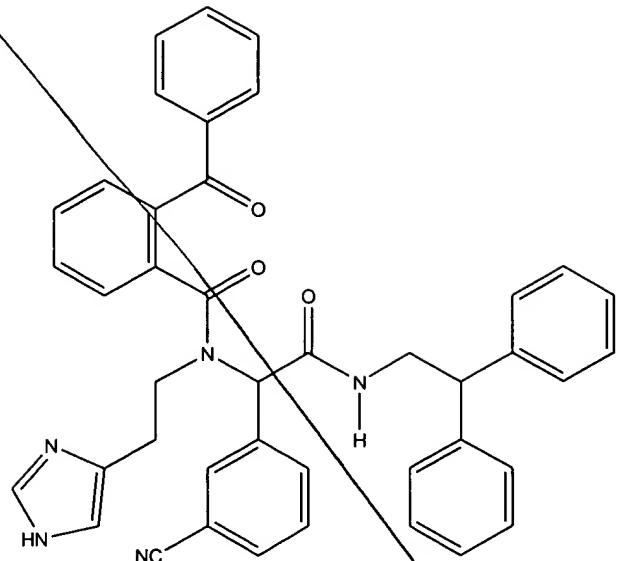
31. A compound which has a positive specific rotation, wherein the compound is represented by the following structural formula:

-90-

*Sub
A³*

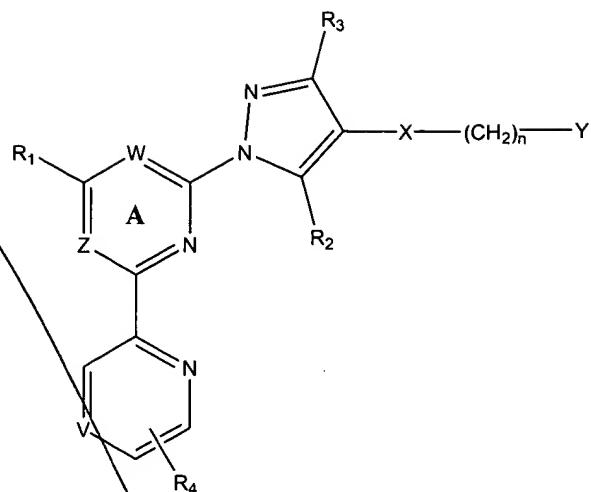
32. A compound which has a negative specific rotation, wherein the compound is represented by the following structural formula:

Sub
A³



33. A method of treating a TNF- α mediated condition in a patient, comprising administering to the patient a therapeutically effective amount of a compound of Formula I,

(I)



and physiological salts thereof, wherein:

n is 0, 1 or 2;

X is O, CH₂, S or SO₂;

R₁ is H or NH₂;

R₂ and R₃ are each, independently, -H, -OH, a substituted or unsubstituted alkyl, or a substituted or unsubstituted alkoxy;

R₄ is, -H or a substituted or unsubstituted alkyl;

V, W and Z are each, independently, N or CH; and

Y is selected from the group consisting of substituted and unsubstituted phenyl, and substituted and unsubstituted heterocyclyl.

34. The method of Claim 33, wherein Y is a phenyl group which has one or more substituents independently selected from the group consisting of halogen, linear or branched C₁-C₄-alkoxy, trifluoromethoxy, dioxymethylene, hydroxyalkyl,

trifluoromethyl, HC(O)-, linear or branched C₁-C₄-alkyl, heterocyclyl and substituted or unsubstituted heterocycloalkylalkyl.

35. The method of Claim 34, wherein Y is a phenyl group which has one or more substituents selected from the group consisting of fluoro, chloro, methoxy, morpholyl, N-morpholinomethyl, tetrahydroisoquinolyl, tetrahydroisoquinolinomethyl, 4-(4-benzyl-piperazin-1-yl)methyl, 4-(4-(2-fluoro-phenyl)piperazin-1-yl)methyl, and isopropyl.

5

36. The method of Claim 33, wherein Y is selected from the group consisting of pyridyl, furyl, and pyrrolidyl.

10

37. The method of Claim 33, wherein the TNF- α mediated condition is selected from the group consisting of acute and chronic immune and autoimmune pathologies.

15

38. The method of Claim 37, wherein the TNF- α mediated condition is selected from the group consisting of systemic lupus erythematosus, rheumatoid arthritis, thyroidosis, graft versus host disease, scleroderma, diabetes mellitus and Graves' disease.

20

39. The method of Claim 33, wherein the TNF- α mediated condition is an infection.

40. The method of Claim 39, wherein the TNF- α mediated condition is selected from the group consisting of sepsis syndrome, cachexia, circulatory collapse and shock resulting from acute or chronic bacterial infection, acute and chronic parasitic, bacterial, viral and fungal infectious diseases.

41. The method of Claim 33, wherein the TNF- α mediated condition is an inflammatory disease.

42. The method of Claim 41, wherein the TNF- α mediated condition is selected from the group consisting of chronic inflammatory pathologies and vascular inflammatory pathologies.

43. The method of Claim 42, wherein the TNF- α mediated condition is selected from the group consisting of sarcoidosis, chronic inflammatory bowel disease, ulcerative colitis, Crohn's disease, disseminated intravascular coagulation, atherosclerosis, and Kawasaki's pathology.

44. The method of Claim 33, wherein the TNF- α mediated condition is a neurodegenerative disease.

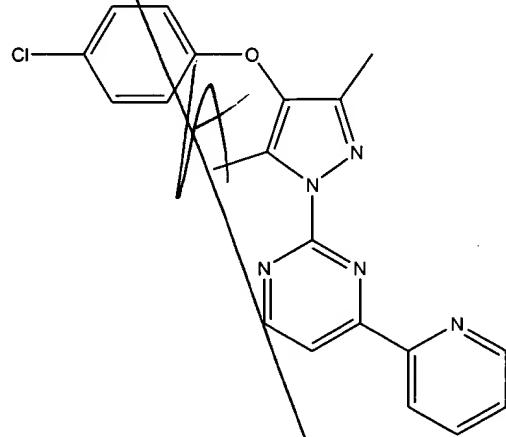
45. The method of Claim 44, wherein the TNF- α mediated condition is selected from the group consisting of multiple sclerosis, acute transverse myelitis, lesions of the corticospinal system, disorders of the basal ganglia or cerebellar disorders, hyperkinetic movement disorders such as Huntington's Chorea and senile chorea, drug-induced movement disorders, hypokinetic movement disorders, progressive supranucleo palsy, astructural lesions of the cerebellum, spinal ataxia, Friedreich's ataxia, cerebellar cortical degenerations, multiple systems degenerations, Refsum's disease, abetalipoproteinemia, ataxia, telangiectasia, mitochondrial multisystem disorder, multiple sclerosis, acute transverse myelitis, neurogenic muscular atrophies, Alzheimer's disease, Down's Syndrome in middle age, Diffuse Lewy body disease, Senile Dementia of Lewy body type, Wernicke-Korsakoff syndrome, chronic alcoholism, Creutzfeldt-Jakob disease, Subacute sclerosing panencephalitis, Hallerorden-Spatz disease, and Dementia pugilistica.

46. The method of Claim 33, wherein the TNF- α mediated condition is cancer.

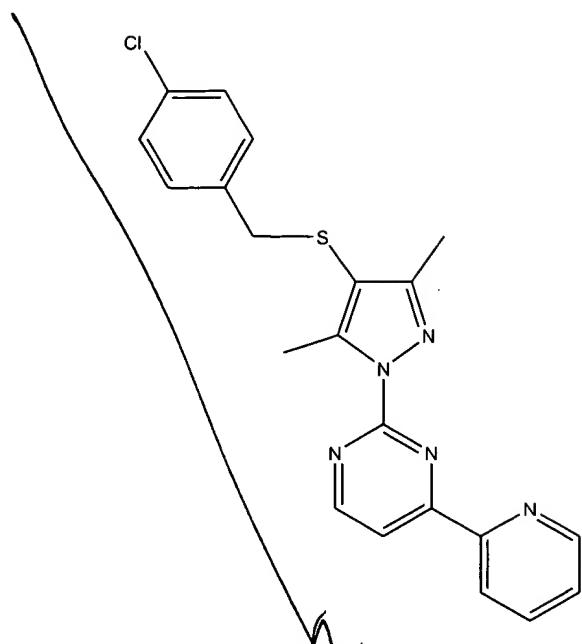
47. The method of Claim 46, wherein the TNF- α mediated condition is selected from the group consisting of TNF- α secreting tumors, leukemias, and lymphomas.

48. The method of Claim 33, wherein the TNF- α mediated condition is alcohol-induced hepatitis.

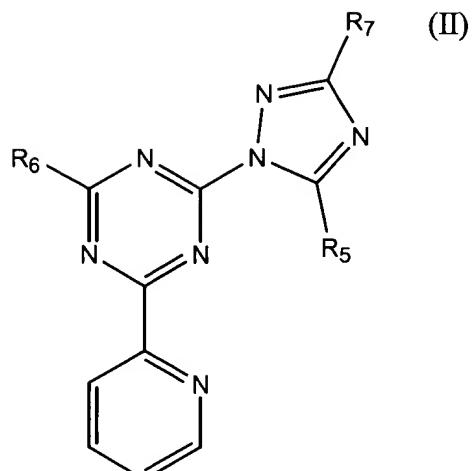
5 49. A method of treating a TNF- α mediated condition in a patient, comprising the step of administering to the patient a therapeutically effective amount of a compound represented by the following structural formula:



10 50. A method of treating a TNF- α mediated condition in a patient, comprising the step of administering to the patient a therapeutically effective amount of a compound represented by the following structural formula:



51. A method of treating a TNF- α mediated condition in a patient, comprising administering to the patient a therapeutically effective amount of a compound of Formula II,



and physiological salts thereof, wherein,

R_5 is substituted or unsubstituted aralkyl, substituted or unsubstituted cycloalkyl, or substituted or unsubstituted cycloalkylalkyl;

5 R_6 is -H or $-NR_{13}R_{14}$;

R_7 is substituted or unsubstituted phenyl; and

R_{13} and R_{14} are each, independently, -H, a substituted or unsubstituted alkyl, a substituted or unsubstituted cycloalkyl, a substituted or unsubstituted aryl, a substituted or unsubstituted aralkyl; or

10 R_{13} and R_{14} together with the nitrogen to which they are attached are a heterocycloalkyl.

52. The method of Claim 51, wherein R_5 is substituted or unsubstituted benzyl.

53. The method of Claim 52, wherein R_5 is benzyl having one or more substituents independently selected from the group consisting of halogen, linear C_1-C_4 -

15 alkoxy and branched C_1-C_4 -alkoxy.

54. The method of Claim 53, wherein R₅ is benzyl having one or more substituents independently selected from the group consisting of chloro and methoxy.

55. The method of Claim 51, wherein R₅ is C₃-C₈-cycloalkyl, C₃-C₈-cycloalkyl-C₁-C₄-alkyl or substituted or unsubstituted phenyl-C₂-C₄-alkyl.

5 56. The method of Claim 54, wherein R₅ is selected from the group consisting of 2-phenethyl, cyclohexyl and cyclopentylethyl.

57. The method of Claim 51, wherein R₇ is phenyl having one or more substituents independently selected from the group consisting of halogen, linear C₁-C₆-alkyl, branched C₁-C₆-alkyl and cyclic C₃-C₆-alkyl and trifluoromethyl.

10 58. The method of Claim 57, wherein R₇ is phenyl having one or more substituents independently selected from the group consisting of fluoro, chloro, linear C₁-C₄-alkyl, and branched C₁-C₄-alkyl.

15 59. The method of Claim 51, wherein the TNF- α mediated condition is selected from the group consisting of acute and chronic immune and autoimmune pathologies.

60. The method of Claim 59, wherein the TNF- α mediated condition is selected from the group consisting of systemic lupus erythematosus, rheumatoid arthritis, thyroidosis, graft versus host disease, scleroderma, diabetes mellitus and Graves' disease.

20 61. The method of Claim 51, wherein the TNF- α mediated condition is an infection.

62. The method of Claim 61, wherein the TNF- α mediated condition is selected from the group consisting of sepsis syndrome, cachexia, circulatory collapse and shock resulting from acute or chronic bacterial infection, acute and chronic parasitic, bacterial, viral and fungal infectious diseases.

5 63. The method of Claim 51, wherein the TNF- α mediated condition is an inflammatory disease.

64. The method of Claim 63, wherein the TNF- α mediated condition is selected from the group consisting of chronic inflammatory pathologies and vascular inflammatory pathologies.

10 65. The method of Claim 64, wherein the TNF- α mediated condition is selected from the group consisting of sarcoidosis, chronic inflammatory bowel disease, ulcerative colitis, Crohn's disease, disseminated intravascular coagulation, atherosclerosis, and Kawasaki's pathology.

66. The method of Claim 51, wherein the TNF- α mediated condition is a neurodegenerative disease.

15 67. The method of Claim 66, wherein the TNF- α mediated condition is selected from the group consisting of multiple sclerosis, acute transverse myelitis, lesions of the corticospinal system, disorders of the basal ganglia or cerebellar disorders, hyperkinetic movement disorders such as Huntington's Chorea and senile chorea, drug-induced movement disorders, hypokinetic movement disorders, progressive supranucleo palsy, astructural lesions of the cerebellum, spinal ataxia, Friedreich's ataxia, cerebellar cortical degenerations, multiple systems degenerations, Refsum's disease, abetalipoproteinemia, ataxia, telangiectasia, mitochondrial multisystem disorder, multiple sclerosis, acute

transverse myelitis, neurogenic muscular atrophies, Alzheimer's disease, Down's Syndrome in middle age, Diffuse Lewy body disease, Senile Dementia of Lewy body type, Wernicke-Korsakoff syndrome, chronic alcoholism, Creutzfeldt-Jakob disease, Subacute sclerosing panencephalitis, Hallerorden-Spatz disease, and Dementia pugilistica.

5

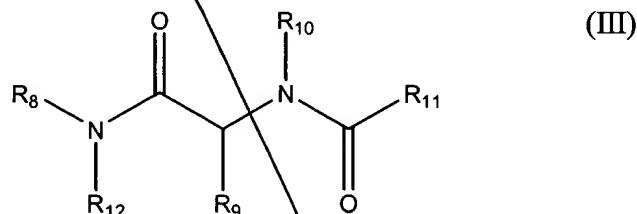
68. The method of Claim 51, wherein the TNF- α mediated condition is cancer.

69. The method of Claim 68, wherein the TNF- α mediated condition is selected from the group consisting of TNF- α secreting tumors, leukemias, and lymphomas.

10 70. The method of Claim 51, wherein the TNF- α mediated condition is alcohol-induced hepatitis.

71. A method of treating a TNF- α mediated condition in a patient, comprising administering to the patient a therapeutically effective amount of a compound of Formula III,

SJ
AK
15



*Sub
A4*

and physiological salts thereof, wherein:

5 ~~R₈ and R₁₂ are each, independently, -H, a substituted or unsubstituted alkyl, a substituted or unsubstituted aryl, substituted or unsubstituted aralkyl or a substituted or unsubstituted heteroaralkyl;~~

10 ~~R₉ is -H, a substituted or unsubstituted aryl, a substituted or unsubstituted aralkyl, a substituted or unsubstituted heteroaryl or a substituted or unsubstituted heteroaralkyl;~~

15 ~~R₁₀ is substituted or unsubstituted alkyl, a substituted or unsubstituted aryl, a substituted or unsubstituted heteroaralkyl, or a substituted or unsubstituted heterocycloalkylalkyl; and~~

20 ~~R₁₁ is a substituted or unsubstituted alkyl, a substituted or unsubstituted aryl, a substituted or unsubstituted aralkyl, a substituted or unsubstituted cycloalkylalkyl, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted heteroaralkyl, a substituted or unsubstituted benzophenyl, or a substituted or unsubstituted cycloalkylalkyl.~~

25 72. The method of Claim 71, wherein one of R₈ or R₁₂ is -H and the other is substituted or unsubstituted phenyl, phenyl-C₁-C₄-alkyl, diphenyl-C₁-C₄-alkyl, linear C₁-C₁₂-alkyl, branched C₁-C₁₂-alkyl, cyclic C₃-C₁₂-alkyl, or dicycloalkyl-C₁-C₄-alkyl.

20 73. The method of Claim 72, wherein one of R₈ or R₁₂ is -H and the other is phenyl, phenyl-C₁-C₄-alkyl, or diphenyl-C₁-C₄-alkyl wherein the phenyl group or phenyl groups bear one or more substituents independently selected from the group consisting of C₁-C₄-alkoxy, C₁-C₄-alkyl and cyano.

25 74. The method of Claim 73, wherein the phenyl group or phenyl groups bear one or more substituents independently selected from the group consisting of methoxy, methyl and cyano.

75. The method of Claim 71, wherein R₈ is selected from the group consisting of 2,2-diphenylethyl, 2-(4-ethylphenyl)ethyl, benzyl, diphenylmethyl, 1,2-diphenylethyl, 3,3-diphenylpropyl, 3,4,5-trimethoxybenzyl, 2,4,4-trimethylisopentyl, 2-(4-methoxyphenyl)ethyl, 2-cyclopentyl-2-phenylethyl, or 2-phenyl-2-pyridylethyl.

5

76. The method of Claim 71 wherein R₉ is substituted or unsubstituted phenyl, phenyl-C₁-C₄-alkyl, diphenyl-C₁-C₄-alkyl, phenylfuranyl or heteroaryl-C₁-C₄-alkyl.

10 77. The method of Claim 76, wherein R₉ is phenyl, phenyl-C₁-C₄-alkyl, diphenyl-C₁-C₄-alkyl wherein the phenyl group or phenyl groups bear one or more substituents independently selected from the group consisting of cyano, C₁-C₄-alkyl-S-, a halogen C₁-C₄-alkyl, C₁-C₄-alkoxy, trifluoromethyl, and substituted and unsubstituted phenoxy.

15 78. The method of Claim 76, wherein R₉ is phenyl, phenyl-C₁-C₄-alkyl, diphenyl-C₁-C₄-alkyl wherein the phenyl group or phenyl groups bear one or more substituents independently selected from the group consisting of cyano, methyl, methoxy, phenoxy, chloro-substituted phenoxy, methoxy-substituted phenoxy and methyl-substituted phenoxy.

20 79. The compound of Claim 71, wherein R₉ is phenyl, 2-cyanophenyl, 3-cyanophenyl, 4-cyanophenyl, diphenylmethyl, pyrazolylmethyl, 2,4-dimethylphenyl, 2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 2-methyl-4-methoxyphenyl, 3-methyl-4-methoxyphenyl, 4-methylthiophenyl, 3-chlorophenyl, 3-trifluoromethylphenyl, benzyl, 2-trifluoromethylbenzyl, 3-trifluoromethylbenzyl, 2-chlorobenzyl, 3-chlorobenzyl, 4-chlorobenzyl, 2-methoxybenzyl, 3-methoxybenzyl, 4-methoxybenzyl, 2-fluorobenzyl, 3-

25

*Su b
P1*

Sub
B1

fluorobenzyl, 4-fluorobenzyl, 3-azidylphenyl, 3-(4-methoxyphenoxy)phenyl, or 5-phenylfuran-2-yl.

Sub
AS

5

80. The method of Claim 71, wherein R₁₀ is substituted or unsubstituted phenyl, alkyl substituted with a heteroaryl group, alkyl substituted with a heterocycloalkyl group, or an alkyl substituted with -NR₁₃R₁₄, wherein:
R₁₃ and R₁₄ are each, independently, -H, a substituted or unsubstituted alkyl, a substituted or unsubstituted cycloalkyl, a substituted or unsubstituted aryl, or a substituted or unsubstituted aralkyl; or
R₁₃ and R₁₄ together with the nitrogen to which they are attached are a heterocycloalkyl.

10

81. The method of Claim 80, wherein R₁₀ is 2-(imidazol-4-yl)ethyl, 3-(imidazol-4-yl)propyl, 3-(imidazol-1-yl)propyl 2-(3-methylimidazol-4-yl)ethyl, 2-(morpholin-4-yl)ethyl, 2-(4-pyrazolyl)ethyl, 4-pyrazolylmethyl, 2-N,N-dimethylaminoethyl, 3-N,N-dimethylaminopropyl, and 2-(aminocarbonyl)phenyl.

15

82. The method of Claim 71, wherein R₁₁ is a linear or branched C₁-C₄-alkyl, substituted or unsubstituted phenyl, substituted or unsubstituted benzophenonyl, pyrazolyl, aminopyrazolyl, substituted or unsubstituted indolyl-C₁-C₄-alkyl, thiophenyl, quinoxaline, substituted or unsubstituted phenyl-C₁-C₄-alkyl, pyridylcarbonylphenyl, phenylcarbonyl-C₁-C₄-alkyl, naphthyl, naphthyl-C₁-C₄-alkyl, diphenyl-C₁-C₄-alkyl, C₅-C₈-cycloalkyl-C₁-C₄-alkyl, C₁-C₄-alkylcarbonyl-C₁-C₄-alkyl, fluorenyl, pryrrolyl, N-methylpyrrolyl, or pyridyl.

20

83. The method of Claim 82, wherein R₁₁ is a phenyl, phenyl-C₁-C₄-alkyl, phenylcarbonyl-C₁-C₄-alkyl, naphthyl-C₁-C₄-alkyl, diphenyl-C₁-C₄-alkyl, C₅-C₈-

cycloalkyl-C₁-C₄-alkyl, fluorenyl or pyridyl substituted with one or more substituents independently selected from C₁-C₄-alkyl and C₁-C₄-alkoxy.

84. The method of Claim 82, wherein R₁₁ is a benzophenonyl group, wherein said benzophenonyl group is substituted with a C₁-C₄-alkoxy group, a C₁-C₄-alkyl group or a chlorine atom.

5

85. The method of Claim 71, wherein R₁₁ is benzophenon-2-yl, 4'-methoxybenzophenon-2-yl, 4'-chlorobenzophenon-2-yl, 2-(furan-2-yl)phenyl, 2-(thiophen-2-yl)phenyl, 2-benzylphenyl, 2-pyridylcarbonylphenyl, 2-(phenoxyethyl)phenyl, 2-(t-butylcarbonyl)phenyl, 2,2-diphenylethyl, 1-fluorenyl, (naphth-2-yl)methyl, naphth-1-yl, 3-(phenylcarbonyl)propyl, 4-phenylbutyl, 4-butylphenyl, 2-(4-chlorophenylcarbonyl)phenyl, 3-methoxyphenyl, N-methylpyrrol-2-yl, 2,3-dimethoxyphenyl, 3-butyl-2-pyridyl, 2-naphthylmethyl, 2-cyclohexylethyl, 3-methoxyphenyl, N-methyl-2-pyrrolyl, 2-cyclopentylethyl, 3-oxobutyl, 2-benzopyrazyl, quinoxalin-2-yl, 3-idolyl, (2-methylindol-3-yl)methyl, 3-(indol-3-yl)propyl, (indol-3-yl)methyl, (5-bromoindol-3-yl)methyl, 3-chlorophenyl, 3-aminopyrazol-4-yl, 2-(indol-3-yl)-1-hydroxyethyl, 3-fluorophenyl, 1-phenyl-1-hydroxymethyl, 2-phenylphenyl, 2-phenoxyphenyl, thiophen-2-yl, or isopropyl.

10

15

20

25

86. The method of Claim 71, wherein the TNF- α mediated condition is selected from the group consisting of acute and chronic immune and autoimmune pathologies.

87. The method of Claim 86, wherein the TNF- α mediated condition is selected from the group consisting of systemic lupus erythematosus, rheumatoid arthritis, thyroidosis, graft versus host disease, scleroderma, diabetes mellitus and Graves' disease.

88. The method of Claim 71, wherein the TNF- α mediated condition is an infection.

89. The method of Claim 88, wherein the TNF- α mediated condition is selected from the group consisting of sepsis syndrome, cachexia, circulatory collapse and shock resulting from acute or chronic bacterial infection, acute and chronic parasitic, bacterial, viral and fungal infectious diseases.
5

90. The method of Claim 71, wherein the TNF- α mediated condition is an inflammatory disease.

91. The method of Claim 90 wherein the TNF- α mediated condition is selected from the group consisting of chronic inflammatory pathologies and vascular inflammatory pathologies.
10

92. The method of Claim 91, wherein the TNF- α mediated condition is selected from the group consisting of sarcoidosis, chronic inflammatory bowel disease, ulcerative colitis, Crohn's disease, disseminated intravascular coagulation, atherosclerosis, and Kawasaki's pathology.

15 93. The method of Claim 71, wherein the TNF- α mediated condition is a neurodegenerative disease.

94. The method of Claim 93, wherein the TNF- α mediated condition is selected from the group consisting of multiple sclerosis, acute transverse myelitis, lesions of the corticospinal system, disorders of the basal ganglia or cerebellar disorders, hyperkinetic movement disorders such as Huntington's Chorea and senile chorea, drug-induced movement disorders, hypokinetic movement disorders, progressive supranucleo palsy, astructural lesions of the cerebellum, spinal ataxia, Friedreich's ataxia, cerebellar cortical degenerations, multiple
20

Su A 6

Sub A6

systems degenerations, Refsum's disease, abetalipoproteinemia, ataxia, telangiectasia, mitochondrial multisystem disorder, multiple sclerosis, acute transverse myelitis, neurogenic muscular atrophies, Alzheimer's disease, Down's Syndrome in middle age, Diffuse Lewy body disease, Senile Dementia of Lewy body type, Wernicke-Korsakoff syndrome, chronic alcoholism, Creutzfeldt-Jakob disease, Subacute sclerosing panencephalitis, Hallerorden-Spatz disease, and Dementia pugilistica.

5

95. The method of Claim 71, wherein the TNF- α mediated condition is cancer.

10

96. The method of Claim 95, wherein the TNF- α mediated condition is selected from the group consisting of TNF- α secreting tumors, leukemias, and lymphomas.

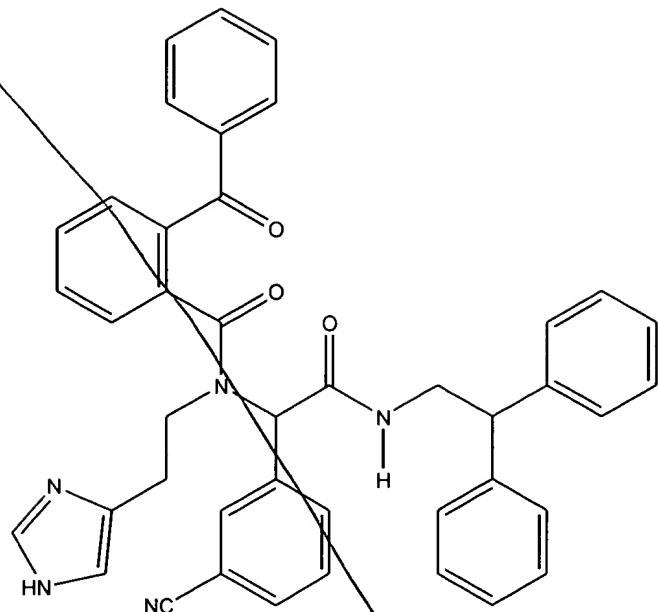
15

97. The method of Claim 71, wherein the TNF- α mediated condition is alcohol-induced hepatitis.

98. A method of treating a TNF- α mediated condition in a patient, comprising the step of administering to the patient a therapeutically effective amount of a compound represented by the following structural formula:

Sub A7

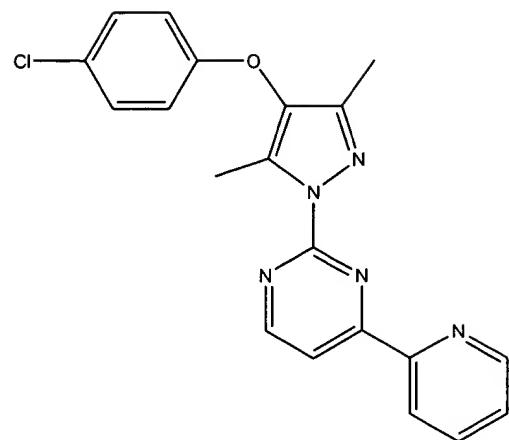
Sub
A7



99. The method of Claim 98, wherein the compound has a positive specific rotation.

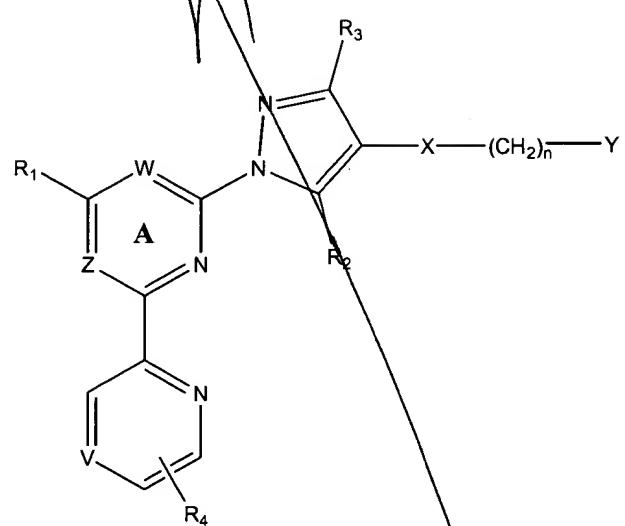
100. The method of Claim 98, wherein the compound has a negative specific rotation.

101. A method of treating multiple sclerosis in a patient, comprising the step of
5 administering to the patient a therapeutically effective amount of a compound
represented by the following structural formula:



102. A compound of Formula I,

(I)



and physiological salts thereof, wherein:

n is 0, 1 or 2;

X is O, CH₂, S or SO₂;

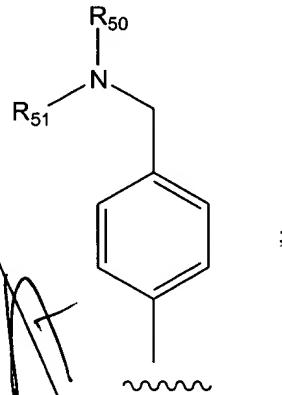
R₁ is H or NH₂;

5 R₂ and R₃ are each, independently, -H, -OH, a substituted or unsubstituted alkyl, or a substituted or unsubstituted alkoxy;

R₄ is, -H or a substituted or unsubstituted alkyl;

V, W and Z are each, independently, N or CH; and

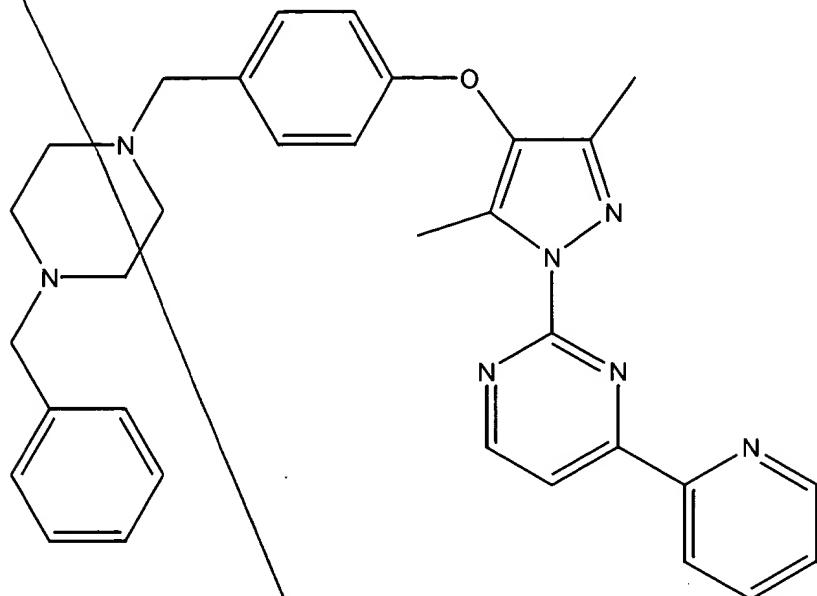
Y is represented by the following structural formula:



10 wherein R₅₀ and R₅₁ are independently an alkyl group, a substituted alkyl group, an aryl group a substituted aryl group, or, taken together with the nitrogen atom to which they are bonded, are a substituted heterocycloalkyl, an unsubstituted heterocycloalkyl, a substituted heteroaryl group or an unsubstituted heteroaryl group.

15 103. A method of treating a TNF- α mediated condition in a patient, comprising administering to the patient a therapeutically effective amount of the compound of Claim 102.

104. A compound represented by the following structural formula:

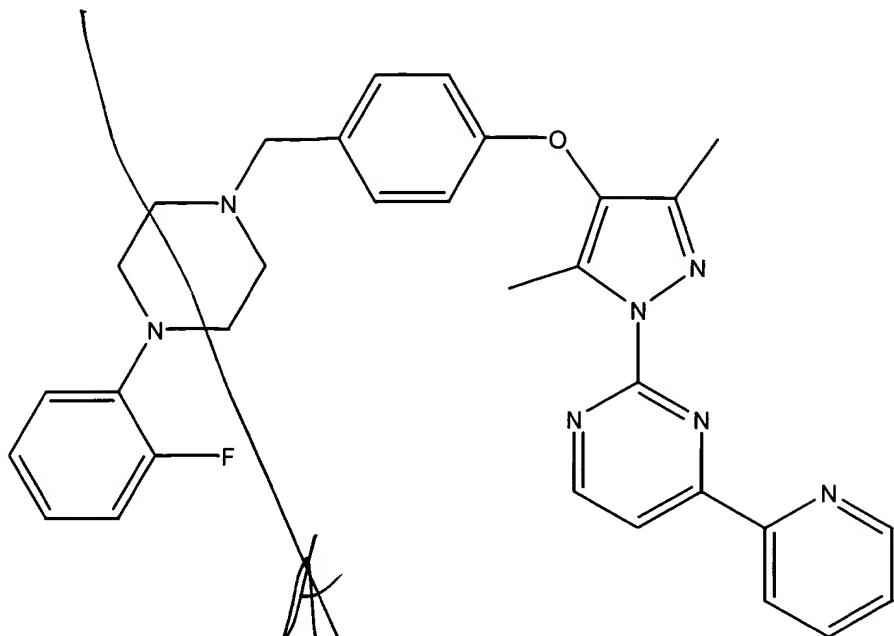


and physiologically acceptable salts thereof.

105. A method of treating a TNF- α mediated condition in a patient, comprising
5 administering to the patient a therapeutically effective amount of the compound
of Claim 104.

106. A compound represented by the following structural formula:

-111-



and physiologically acceptable salts thereof.

107. A method of treating a TNF- α mediated condition in a patient, comprising administering to the patient a therapeutically effective amount of the compound of Claim 106.

5

add
A8